Supplement 4

USP XX
NF XV

Contents

UNITED STATES PHARMACOPEIAL CONVENTION
1980–1985

Officers

FREDERICK E. SHIDEMAN, M.D., PH.D.
President
Minneapolis, Minn.

HARRY C. SHIRKEY, M.D.
Vice-President
Highland Heights, Ky.

PAUL F. PARKER, D.SC.
Treasurer
Lexington, Ky.

JOHN A. OWEN, JR., M.D.
Past President
Charlottesville, Va.

WILLIAM M. HELLER, PH.D.
Secretary
Rockville, Md.

Board of Trustees

WILLIAM J. KINNARD, JR., PH.D.[1]
Chairman
Baltimore, Md.

WILLIAM H. BARR, PHARM.D., PH.D.[1]
Richmond, Va.

JOHN T. FAY, PH.D.[2]
San Francisco, Calif.

PETER GOLDMAN, M.D.[3]
(1981–)
Boston, Mass.

FELIX B. GORRELL[4]
(1981–)
Arlington, Va.

ARTHUR HULL HAYES, JR., M.D.[3]
(1980–1981)
Hershey, Pa.

LEO E. HOLLISTER, M.D.[3]
Palo Alto, Calif.

IRWIN J. LERNER[2]
Nutley, N. J.

JOHN A. OWEN, JR., M.D.
ex officio
Charlottesville, Va.

PAUL F. PARKER, D.SC.
ex officio
Lexington, Ky.

FREDERICK E. SHIDEMAN, M.D., PH.D.
ex officio
Minneapolis, Minn.

HARRY C. SHIRKEY, M.D.
ex officio
Highland Heights, Ky.

General Committee of Revision

WILLIAM M. HELLER, PH.D., *Executive Director, USPC*, 12601 Twinbrook Parkway, Rockville, Md. 20852
Chairman, ex officio

LEE T. GRADY, PH.D.[5]
Director, Drug Standards Division

KEITH W. JOHNSON[5]
Director, Research and Development, Drug Information Division

FAYE G. ABDELLAH
(1981–)
Rockville, Md.

THOMAS J. AMBROSIO, PH.D.
Somerville, N. J.

WILLIAM F. APPEL, B.S.
Minneapolis, Minn.

NORMAN W. ATWATER, PH.D.
Princeton, N. J.

GILBERT S. BANKER, PH.D.
West Lafayette, Ind.

JOHN V. BERGEN, PH.D.
Villanova, Pa.

JOSEPH R. BIANCHINE, PH.D., M.D.
Columbus, Ohio

MARTIN I. BLAKE, PH.D.
Skokie, Ill.

S. GAYLEN BRADLEY, PH.D.
Richmond, Va.

LYNN R. BRADY, PH.D.
Seattle, Wash.

EDWIN D. BRANSOME, JR., M.D.
Augusta, Ga.

WILLIAM H. BRINER, CAPT., B.S.
Durham, N. C.

LARRY C. CAREY, M.D.
Columbus, Ohio

HERBERT S. CARLIN, M.SC.
Chappaqua, N. Y.

D. MARTIN CARTER, M.D., PH.D.
New York, N. Y.

LESTER CHAFETZ, PH.D.
Morris Plains, N. J.

LESLIE G. CHATTEN, PH.D.
Edmonton, Alberta, Canada

SEBASTIAN G. CIANCIO, D.D.S.
Buffalo, N. Y.

EDWARD F. CLEARY, B.S.
Sandy, Utah

JORDAN L. COHEN, PH.D.
Los Angeles, Calif.

WALTER D. CONWAY, PH.D.
Amherst, N. Y.

---

[1] Representing pharmacy.
[2] At large.
[3] Representing medicine.
[4] Public member.
[5] 12601 Twinbrook Parkway, Rockville, Md. 20852.

MURRAY DAVIDSON, M.D.
Jamaica, N. Y.

LLOYD E. DAVIS, D.V.M., PH.D.
Urbana, Ill.

JOHN S. DERRYBERRY, M.D.
Shelbyville, Tenn.

WILLIAM R. EBERT, PH.D.
(1980–1982)
Clearwater, Fla.

CLYDE R. ERSKINE, B.S., M.B.A.
Philadelphia, Pa.

DAVID N. F. FAIRBANKS, M.D.
(1981–)
Bethesda, Md.

EUGENE FARKAS, PH.D.
(1980–1982)
Indianapolis, Ind.

HARRY W. FISCHER, M.D.
Rochester, N. Y.

EDWARD A. FITZGERALD, PH.D.
Bethesda, Md.

KLAUS G. FLOREY, PH.D.
New Brunswick, N. J.

WILLIAM O. FOYE, PH.D.
Boston, Mass.

EDWARD D. FROHLICH, M.D.
New Orleans, La.

SALVATORE A. FUSARI, PH.D.
Morris Plains, N. J.

JOSEPH F. GALLELLI, PH.D.
Bethesda, Md.

ALAN GRAY, PH.D.
West Point, Pa.

MARVIN F. GROSTIC, PH.D.
Kalamazoo, Mich.

J. KEITH GUILLORY, PH.D.
Iowa City, Iowa

LOUIS S. HARRIS, PH.D.
Richmond, Va.

DAVID W. HUGHES, PH.D.
Ottawa, Ontario, Canada

RODNEY D. ICE, PH.D.,
Oklahoma City, Okla.

HERBERT E. KAUFMAN, M.D.
New Orleans, La.

DONALD KAYE, M.D.
Philadelphia, Pa.

B. J. KENNEDY, M.D.
Minneapolis, Minn.

LLOYD KENNON, PH.D.
Ocean City, N. J.

BOEN T. KHO, PH.D.
Rouses Point, N. Y.

LEWIS J. LEESON, PH.D.
(1982–)
Summit, N. J.

ROBERT D. LINDEMAN, M.D.
Louisville, Ky.

MICHAEL D. LOBERG, PH.D.
New Brunswick, N. J.

JENNIFER LOGGIE, M.B., B.CH.
Cincinnati, Ohio

WILLIAM J. MADER, M.S.
Sugarloaf Shores, Fla.

JOHN R. MARKUS, B.S.
Rockville, Md.

THOMAS MEDWICK, PH.D.
Piscataway, N. J.

ROSCOE E. MILLER, M.D.
Indianapolis, Ind.

JOSEPH A. MOLLICA, PH.D.
Summit, N. J.

FRED A. MORECOMBE, B.S.
Mesa, Ariz.

ROBERT F. MORRISSEY, PH.D.
Somerville, N. J.

JAMES W. MUNSON, PH.D.
Kalamazoo, Mich.

HAROLD R. NACE, PH.D.
Barrington, R. I.

WENDEL L. NELSON, PH.D.
Seattle, Wash.

JOHN L. NEUMEYER, PH.D.
Boston, Mass.

JENNIFER R. NIEBYL, M.D.
Baltimore, Md.

STANLEY P. OWEN, PH.D.
Kalamazoo, Mich.

ROBERT V. PETERSEN, PH.D.
Salt Lake City, Utah

EDWARD L. PRATT, B.S.
Rensselaer, N. Y.

JAMES R. RANKIN, B.S.
Taos, N. M.

BARBARA K. REDMAN, PH.D.
(1980–1981)
Washington, D. C.

CHRISTOPHER T. RHODES, PH.D.
Kingston, R. I.

JAY ROBERTS, PH.D.
(1981–)
Philadelphia, Pa.

JOSEPH R. ROBINSON, PH.D.
Madison, Wis.

BRUCE C. RUDY, PH.D.
Dallas, Texas

ANDREW J. SCHMITZ, JR., M.S.
New York, N. Y.

STEPHEN G. SCHULMAN, PH.D.
Gainesville, Fla.

MYRON G. SCHULTZ, D.V.M., M.D.
Atlanta, Ga.

RALPH F. SHANGRAW, PH.D.
Baltimore, Md.

ALBERT L. SHEFFER, M.D.
Boston, Mass.

JANE C. SHERIDAN, PH.D.
Nutley, N. J.

JOSEPH E. SINSHEIMER, PH.D.
Ann Arbor, Mich.

E. JOHN STABA, PH.D.
Minneapolis, Minn.

JAMES T. STEWART, PH.D.
Athens, Ga.

EUGENE A. TIMM, PH.D.
Morristown, N. J.

MURRAY M. TUCKERMAN, PH.D.
Philadelphia, Pa.

SAMUEL M. TUTHILL, PH.D.
St. Louis, Mo.

GERALD W. WALLACE, PH.D.
(1982–)
Indianapolis, Ind.

WALTER L. WAY, M.D.
San Francisco, Calif.

ROBERT G. WOLFANGEL, PH.D.
St. Louis, Mo.

MILTON D. YUDIS, PH.D.
Bloomfield, N. J.

JOHN E. ZAREMBO, PH.D.
Tuckahoe, N. Y.

Executive Committee of Revision (1982–1983)

WILLIAM H. BRINER, CAPT., B.S.
HERBERT S. CARLIN, M.SC.
LESTER CHAFETZ, PH.D.
WILLIAM M. HELLER, PH.D., *Chairman*
ROBERT V. PETERSEN, PH.D.
JAMES R. RANKIN, B.S.
ALBERT L. SHEFFER, M.D.

Division Executive Committees and Subcommittees

Drug Standards Division Subcommittees for 1980–1985

WILLIAM M. HELLER, PH.D., *Chairman of the Drug Standards Division Executive Committee*

The Chairmen of the Subcommittees and, ex officio, the Executive Director, constitute the Drug Standards Division Executive Committee.

ANT. Antibiotics
KLAUS G. FLOREY, PH.D., *Chairman*
Lynn R. Brady, Ph.D.; Salvatore A. Fusari, Ph.D.; David W. Hughes, Ph.D.; Donald Kaye, M.D.

B&M. Biochemistry and Microbiology
EUGENE A. TIMM, PH.D., *Chairman*
S. Gaylen Bradley, Ph.D.; Edwin D. Bransome, Jr., M.D.; Edward A. Fitzgerald, Ph.D.; Alan Gray, Ph.D.; Andrew J. Schmitz, Jr.

CH1. Chemistry
LESTER CHAFETZ, PH.D., *Chairman*
William O. Foye, Ph.D.; James W. Munson, Ph.D.; Harold R. Nace, Ph.D.; John L. Neumeyer, Ph.D.; Milton D. Yudis, Ph.D.

CH2. Chemistry
MARTIN I. BLAKE, PH.D., *Chairman*
Walter D. Conway, Ph.D.; Boen T. Kho, Ph.D.; Fred A. Morecombe; Edward L. Pratt; James T. Stewart, Ph.D.; Samuel M. Tuthill, Ph.D.

CH3. Chemistry
NORMAN W. ATWATER, PH.D., *Chairman*
Leslie G. Chatten, Ph.D.; J. Keith Guillory, Ph.D.; Joseph A. Mollica, Ph.D.; Wendel L. Nelson, Ph.D.; Stephen G. Schulman, Ph.D.

CH4. Natural Products
BRUCE C. RUDY, PH.D., *Chairman*
John V. Bergen, Ph.D.; Eugene Farkas, Ph.D. (1980–1982); Joseph E. Sinsheimer, Ph.D.; E. John Staba, Ph.D.; Gerald W. Wallace, Ph.D. (1982–); John E. Zarembo, Ph.D.

C&S. Containers and Stability
THOMAS MEDWICK, PH.D., *Chairman*
Thomas J. Ambrosio, Ph.D.; William F. Appel; John V. Bergen, Ph.D.; Herbert S. Carlin; Clyde R. Erskine

GEN. General Chapters
MURRAY M. TUCKERMAN, PH.D., *Chairman*
Walter D. Conway, Ph.D.; Marvin F. Grostic, Ph.D.; Thomas Medwick, Ph.D.; Fred A. Morecombe; Edward L. Pratt; Samuel M. Tuthill, Ph.D.

M&S. Medical and Surgical Products
STANLEY P. OWEN PH.D., *Chairman*
Larry C. Carey, M.D.; Edward F. Cleary; Harry W. Fischer, M.D.; Michael D. Loberg, Ph.D.; Robert V. Petersen, Ph.D.

PAR. Parenteral Products
JOSEPH F. GALLELLI, PH.D., *Chairman*
Faye G. Abdellah (1981–); Herbert S. Carlin; Edward F. Cleary; William J. Mader; Robert F. Morrissey, Ph.D.; Barbara K. Redman, Ph.D. (1980–1981); Andrew J. Schmitz, Jr.

PH1. Pharmaceutic Ingredients
RALPH F. SHANGRAW, PH.D., *Chairman*
Gilbert S. Banker, Ph.D.; William R. Ebert, Ph.D. (1980–1982); Lloyd Kennon, Ph.D.; Lewis J. Leeson, Ph.D. (1982–); William J. Mader; Joseph R. Robinson, Ph.D.

PH2. Pharmaceutics—Dosage Forms and Systems
ROBERT V. PETERSEN, PH.D., *Chairman*
William R. Ebert, Ph.D. (1980–1982); Lloyd Kennon, Ph.D.; Lewis J. Leeson, Ph.D. (1982–); Joseph R. Robinson, Ph.D.

PH3. Pharmaceutics—Dissolution
JANE C. SHERIDAN, PH.D., *Chairman*
Jordan L. Cohen, Ph.D.; Christopher T. Rhodes, Ph.D.

RAD. Radiopharmaceuticals
WILLIAM H. BRINER, *Chairman*
Rodney D. Ice, Ph.D.; Michael D. Loberg, Ph.D.; Roscoe E. Miller, M.D.; Robert G. Wolfangel, Ph.D.

VET. Veterinary Products
MARVIN F. GROSTIC, PH.D., *Chairman*
Lloyd E. Davis, D.V.M., Ph.D.; Alan Gray, Ph.D.; John R. Markus; Myron G. Schultz, D.V.M., M.D.; Milton D. Yudis, Ph.D.

Drug Information Division Subcommittees for 1980–1985

WILLIAM M. HELLER, PH.D., *Chairman of the Drug Information Division Executive Committee*

Faye G. Abdellah (1981–), William F. Appel, Martin I. Blake, Ph.D., Edwin D. Bransome, Jr., M.D., Herbert S. Carlin, Sebastian G. Ciancio, D.D.S., Lloyd E. Davis, D.V.M., Ph.D., Jennifer Loggie, M.B., B.Ch., James R. Rankin, Barbara K. Redman, Ph.D. (1980–1981), Albert L. Sheffer, M.D., and, ex officio, the Executive Director, constitute the Drug Information Division Executive Committee.

Consumer Interest
JAMES R. RANKIN, *Chairman*
Faye G. Abdellah (1981–); William F. Appel; Sebastian G. Ciancio, D.D.S.; Barbara K. Redman, Ph.D. (1980–1981); Albert L. Sheffer, M.D.

Drug Distribution
HERBERT S. CARLIN, *Chairman*
Faye G. Abdellah (1981–); Thomas J. Ambrosio, Ph.D.; William F. Appel; Sebastian G. Ciancio, D.D.S.; Lloyd E. Davis, D.V.M., Ph.D.; John S. Derryberry, M.D.; Robert V. Petersen, Ph.D.; Barbara K. Redman, Ph.D. (1980–1981)

Therapeutics I
EDWIN D. BRANSOME, JR., M.D., *Chairman*
Murray Davidson, M.D.; John S. Derryberry, M.D.; Harry W. Fischer, M.D.; Louis S. Harris, Ph.D.; Roscoe E. Miller, M.D.; Jennifer R. Niebyl, M.D.

Therapeutics II
ALBERT L. SHEFFER, M.D., *Chairman*
D. Martin Carter, M.D., Ph.D.; Herbert E. Kaufman, M.D.; Donald Kaye, M.D.; Myron G. Schultz, D.V.M., M.D.

Therapeutics III
JENNIFER LOGGIE, M.B., B.CH., *Chairman*
Joseph R. Bianchine, Ph.D., M.D.; Larry C. Carey, M.D.; Edward D. Frohlich, M.D.; B. J. Kennedy, M.D.; Robert D. Lindeman, M.D.; Walter L. Way, M.D.

Admissions

New Monographs Appearing in This Supplement

USP XX

Acetaminophen and Aspirin Tablets
Acetylcholine Chloride
Acetylcholine Chloride for Ophthalmic Solution
Alumina, Magnesia, and Calcium Carbonate Oral Suspension
Alumina, Magnesia, and Calcium Carbonate Tablets
Amiloride Hydrochloride
Amiloride Hydrochloride Tablets
Amiloride Hydrochloride and Hydrochlorothiazide Tablets
Sterile Ampicillin
Calcium and Magnesium Carbonates Tablets
Calcium Carbonate and Magnesia Tablets
Cefamandole Sodium for Injection
Sterile Cefamandole Sodium
Cephacetrile Sodium
Cephacetrile Sodium for Injection
Chlorzoxazone and Acetaminophen Tablets
Dexpanthenol
Dextrose and Potassium Chloride Injection
Sterile Doxycycline Hyclate
Magnesium Carbonate and Sodium Bicarbonate for Oral Suspension
Manganese Sulfate
Manganese Sulfate Injection
Methenamine Mandelate for Oral Solution
Metronidazole Injection
Sterile Minocycline Hydrochloride
Nystatin for Oral Suspension
Penicillamine Tablets
Chromic Phosphate P 32 Suspension
Tetracycline Hydrochloride Ointment
Sterile Tetracycline Hydrochloride
Sterile Tetracycline Phosphate Complex

NF XV

Polypropylene Glycol

Important—New Changes Adopted Since the Previous Supplement and Addendum and the Fourth Through the Seventh Interim Revision Announcements Were Published Pertain to the Following Titles.

ANNOTATED LIST

General Notices, Monographs, General Chapters, Reagents, and Tables Affected by Changes Appearing in This Supplement

Page citations refer to the pages of this Supplement. Note—The absence of a parenthetic term after the section heading denotes a change in the text, as distinguished from a newly added or deleted section.

General Notices and Requirements (USP XX)

Monographs (USP XX)

General Chapters

General Tests and Assays

General Requirements for Tests and Assays

Microbiological Tests

Chemical Tests and Assays

IDENTIFICATION TESTS

LIMIT TESTS

Physical Tests and Determinations

General Information

Reagents, Indicators, and Solutions

Reagents

REAGENT SPECIFICATIONS

Solutions

TEST SOLUTIONS

Reagent Footnotes, 757

Reference Tables

FOURTH SUPPLEMENT

to USP XX and to NF XV

IMPORTANT—Save the Third Supplement and its Addendum *a*, published February 15 and June 30, 1982, respectively. This Fourth Supplement is **not cumulative** and does not incorporate the content of previous supplements to USP XX-NF XV, except that it does incorporate the content of all Interim Revision Announcements published since the Third Supplement was issued.

This Fourth Supplement and succeeding supplements will add onto the Third Supplement and its Addendum *a;* thus, all of these are needed to keep the compendia up to date.

The index of this Supplement is cumulative from 1980, to facilitate reference to all changes and additions to USP XX-NF XV to date.

Explanation of Symbols—

Document	*Official Date*	*Symbols*
First Supplement to USP XX and to NF XV	July 1, 1980	■ and ■1
Addendum *a* to the above	July 1, 1980	▲ and ▲1a
First Interim Revision Announcement	July 1, 1980	● and ●1
Second Supplement	May 1, 1981	■ and ■2
Second Interim Revision Announcement	May 1, 1981	● and ●2
Addendum *a* to Second Supplement	Nov. 1, 1981	▲ and ▲2a
Third Interim Revision Announcement	Nov. 1, 1981	● and ●3
Fourth Interim Revision Announcement	March 1, 1982	● and ●4
Third Supplement	May 1, 1982	■ and ■3
Fifth Interim Revision Announcement	May 1, 1982	● and ●5
Addendum *a* to Third Supplement	Sept. 1, 1982	▲ and ▲3a
Sixth Interim Revision Announcement	Sept. 1, 1982	● and ●6
Seventh Interim Revision Announcement	Sept. 1, 1982	● and ●7
Fourth Supplement	May 1, 1983	■ and ■4

Superscript symbol denotes the start of a change; *subscript* symbol with numeral or numeral and letter denotes the end of a change.

Where the superscript and subscript symbols appear together with no intervening text, it means that a word or words have simply been deleted.

The figure(s) following a subscript symbol also denote the official date of the change; thus, the numeral "1" refers to the *First* Supplement, and by inference denotes the official date July 1, 1980.

Introduction

Changes and additions listed herein constitute revisions in USP XX and in NF XV effective May 1, 1983, except where otherwise noted.

This combined USP and NF Supplement is arranged in the order in which the items appear in the USP XX-NF XV main volume.

The Third Supplement comprises pages 1-440 and its Addendum *a* comprises pages 441-654; this Supplement starts with page 655, and includes an index that pertains to the Third Supplement and its Addendum *a* and to this Supplement.

The format and general editorial style employed in the Supplement serve not only for printing convenience but also for accommodation to computer storage and retrieval processes.

Official Title Changes—NOTE—In all instances where "*Monograph title change (see Note in Introduction)*" is specified, it is to be understood that the official title given after that specification is to be substituted for the former title in the appropriate places throughout the monograph concerned.

In succeeding Supplements, further revisions of the monograph concerned will be shown under the new, currently official title in its respective alphabetic position.

USP XX and NF XV are published by the U. S. Pharmacopeial Convention, Inc., 12601 Twinbrook Pkwy., Rockville, MD 20852. The USP XX-NF XV main volume is distributed for USPC by the Mack Printing Co., Easton, PA 18042.

All correspondence and suggestions for revisions with respect to either USP or NF should be addressed to: Drug Standards Division, USP-NF, 12601 Twinbrook Pkwy., Rockville, MD 20852.

USP XX
General Notices *and* Requirements

"OFFICIAL" AND "OFFICIAL ARTICLES"

Change to read:

The word "official," as used in this Pharmacopeia or with reference hereto, is synonymous with "Pharmacopeial," with "USP," and with "compendial."

The designation USP in conjunction with the official title on the label of an article is a reminder that the article purports to comply with USP standards; such specific designation on the label does not constitute a representation, endorsement, or incorporation by the manufacturer's labeling of the informational material contained in the USP monograph, nor does it constitute assurance by USP that the article is known to comply with USP standards. The standards apply equally to articles bearing the official titles or names derived by transposition of the definitive words of official titles, whether or not the added designation "USP" is used. Names considered to be synonyms of the official titles may not be used for official titles.

Where a product differs from the standards of strength, quality, and purity, ■as determined by the application of the assays and tests,■4 set forth for it in the Pharmacopeia, its difference shall be plainly stated on its label. Where a product fails to comply in identity with the identity prescribed in the USP, ■or contains an added substance that interferes with the prescribed assays and tests,■4 such product shall be designated by a name that is clearly distinguishing and differentiating from any name recognized in the Pharmacopeia.

Articles listed herein are official and the standards set forth in the monographs apply to them only when the articles are intended or labeled for use as drugs or medical devices and when bought, sold, or dispensed for these purposes.

An article is deemed to be recognized in this Pharmacopeia when a monograph for the article is published in it, including its supplements, addenda, or other interim revisions, and an official date is generally or specifically assigned to it.

The following terminology is used for distinguishing the articles for which monographs are provided: an *official substance* is an active drug entity or a pharmaceutic ingredient or a component of a finished device for which the monograph title includes no indication of the nature of the finished form; a *dosage form* or a *finished device* is the finished, or partially finished (e.g., as in the case of a sterile solid to be constituted into a solution for administration), preparation or product of one or more official substances formulated for use on or for the patient; an *article* is an item for which a monograph is provided, whether an official substance, a dosage form, or a finished device.

ABBREVIATIONS

Change to read:

The expression FDA refers to the U. S. Food and Drug Administration; NBS refers to the National Bureau of Standards. The expression FCC refers to the current edition of the Food Chemicals Codex, including its supplements. The term PhI refers to the International Pharmacopoeia,* published as a recommendation on international standards of strength, quality, and purity for drugs by the World Health Organization. The expressions ACS, ANSI, AOAC, and ASTM refer, respectively, to the American Chemical Society, the American National Standards Institute, the Association of Official Analytical Chemists, and the American Society for Testing and Materials.

■The term RS refers to Reference Standard as stated under *Reference Standards* in the General Notices.■4

The terms CS and TS refer to Colorimetric Solution and Test Solution, respectively (see under *Reagents, Indicators, and Solutions*). ■The term VS refers to Volumetric Solution as stated under *Solutions* in the General Notices.■4

Abbreviated Statements in Monographs—Incomplete sentences are employed in various portions of the monographs for directness and brevity. Where the limit tests are so abbreviated, it is to be understood that the chapter numbers (shown in angle brackets) designate the respective procedures to be followed, and that the values specified after the colon are the required limits.

INGREDIENTS AND PROCESSES

Change to read:

Added Substances—An official substance, as distinguished from a dosage form, contains no added substances except where specifically permitted in the individual monograph. Where such addition is permitted, the label indicates the name(s) and amount(s) of any added substance(s).

Unless otherwise specified in the individual monograph, or elsewhere in the General Notices, suitable substances such as bases, carriers, coatings, colors, flavors, preservatives, stabilizers, and vehicles may be added to a Pharmacopeial dosage form or finished de-

* With the publication of the Second Edition of the International Pharmacopoeia, *Specifications for the Quality Control of Pharmaceutical Preparations* was shown as its primary title; however, the short title is used also.

vice to enhance its stability, usefulness, or elegance, or to facilitate its preparation. Such substances ■are regarded as unsuitable and are prohibited unless (a)■4 they are harmless in the amounts used, ■(b)■4 they do not exceed the minimum quantity required to provide their intended effect, ■(c)■4 their presence does not impair the bioavailability or the therapeutic efficacy of the dosage form, and ■(d)■4 they do not interfere with the assays and tests prescribed for determining compliance with the Pharmacopeial standards.

Colors—Added substances employed solely to impart color may be incorporated into Pharmacopeial articles that are dosage forms or finished devices, except those intended for parenteral or ophthalmic use, in accordance with the regulations pertaining to the use of colors in drugs issued by the Food and Drug Administration, provided such added substances are otherwise appropriate in all respects. (See also *Added Substances* under *Injections* ⟨1⟩.)

Capsules and Tablets—Capsules and tablets may be made with suitable diluents, colors, lubricants, disintegrants, and adhesives, such as starches, lactose, sucrose, and other innocuous materials. Tablets and the contents of capsules that are intended to be homogeneous are uniform in appearance within a given lot. Excessive amounts of substances that may impair bioavailability of the active ingredients are to be avoided. Tablets may be coated.

Parenteral and Topical Preparations—For the preservation of preparations intended for parenteral administration or topical application, suitable antioxidants, antimicrobial agents, buffers, and/or stabilizers may be added unless interdicted in the monograph.

For requirements concerning the presence and proportions of added substances in parenteral preparations, and the pertinent labeling requirements, see *Added Substances* and *Labeling* under *Injections* ⟨1⟩.

The air in a container of an article for parenteral use may be evacuated or be replaced by carbon dioxide, helium, or nitrogen, or by a mixture of these gases, which fact need not be declared on the label unless otherwise specified in the individual monograph.

Ointments and Suppositories—In the preparation of ointments and suppositories, the proportions of the substances constituting the base may be varied to maintain a suitable consistency under different climatic conditions, provided the concentrations of active ingredients are not varied.

PRESERVATION, PACKAGING, STORAGE, AND LABELING

Change to read:

Labeling—■The term "labeling" designates all labels and other written, printed, or graphic matter upon an immediate container of an article or upon, or in, any package or wrapper in which it is enclosed, except any outer shipping container. The term "label" designates that part of the labeling upon the immediate container.

A shipping container, unless such container is also essentially the immediate container or the outside of the consumer package, is exempt from the labeling requirements of this Pharmacopeia.

Articles in this Pharmacopeia are subject to compliance with such labeling requirements as may be promulgated by federal regulations in addition to the Pharmacopeial requirements set forth for the articles.

The potency of some antibiotics, as well as of relatively new drugs generally, is defined in terms of μg or mg of the parent drug (i.e., that portion of the compound which conveys the qualitative pharmacologic activity), even though the antibiotic or other drug used in the dosage form may be in the form of a salt, ester, or other chemical combination. The full name of the chemical combination is used in the content declaration.■4

Amount of Ingredient per Dosage Unit—Pharmacopeial articles in capsule, tablet, or other unit dosage form shall be labeled to express the quantity of each therapeutically active ingredient contained in each such unit. Pharmacopeial articles not in unit dosage form shall be labeled to express the quantity of each therapeutically active ingredient in each ml or in each g, or to express the percentage of each such ingredient (see *Percentage Measurements*), except that oral liquids may, alternatively, be labeled in terms of each 5-ml portion.

Labeling Parenteral and Topical Preparations—The label of a preparation intended for parenteral or topical use states the names of all added substances (see *Added Substances*, in these General Notices, and *Labeling* under *Injections* ⟨1⟩), and, in the case of parenteral preparations, also their amounts or proportions, except that for substances added for adjustment of pH or to achieve isotonicity, the label may indicate only their presence and the reason for their addition.

Labeling Vitamin-containing Products—The vitamin content of Pharmacopeial preparations shall be stated on the label in metric units. The amounts of vitamins A, D, and E may be stated also in USP Units. Quantities of vitamin A declared in metric units refer to the equivalent amounts of retinol (vitamin A alcohol).

Labeling Electrolytes—The concentration and dosage of electrolytes for replacement therapy (e.g., sodium chloride or potassium chloride) shall be stated on the label in milliequivalents (mEq). The label of the product shall indicate also the quantity of ingredient(s) in terms of weight or percentage concentration.

Special Capsules and Tablets—The label of any form of Capsule or Tablet intended for administration other than by swallowing intact bears a prominent indication of the manner in which it is to be used. Where a tablet is enteric-coated, the label so states.

Change to read:

Expiration Date—The labels of all Pharmacopeial dosage forms ■■1 shall bear an expiration date. The monographs for some dosage forms ■■1 specify the expiration date that shall appear on the label. In the absence of a specific requirement in the individual monograph for a dosage form, ■■1 the label shall bear an expiration date assigned for the particular formu-

lation and package of the article, ■with the following exception: The label need not show an expiration date in the case of a dosage form packaged in a container that is intended for sale without prescription and the labeling of which states no dosage limitations, and which is stable for not less than 3 years when stored under the prescribed conditions. The expiration■4 date identifies the time during which the article may be expected to meet the requirements of the Pharmacopeial monograph provided it is kept under the prescribed storage conditions. The expiration date limits the time during which the product may be dispensed or used. Where an expiration date is stated only in terms of the month and the year, it is a representation that the intended expiration date is the last day of the stated month. For articles requiring constitution prior to use, a suitable beyond-use date for the constituted product shall be identified in the labeling.

USP XX Monographs

In the following monograph, the *Dissolution* test is not official at this time. (Via the Seventh Interim Revision Announcement, the *Dissolution* test in this monograph is being held in abeyance until further notice.)

Glutethimide Tablets, page 526 of Addendum *a* to the Third Supplement.

Acetaminophen Elixir

Change to read:

Packaging and storage—Preserve in tight containers. ■4

Add the following:

■Acetaminophen and Aspirin Tablets

» Acetaminophen and Aspirin Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$).

Packaging and storage—Preserve in tight containers.

Reference standards—*USP Acetaminophen Reference Standard*—Dry over silica gel for 18 hours before using. *USP Aspirin Reference Standard*—Dry over silica gel for 5 hours before using. *USP Salicylic Acid Reference Standard*—Dry over silica gel for 3 hours before using.

Identification—The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those of the *Standard preparation*, relative to the internal standard, as obtained in the *Assay*.

Weight variation ⟨931⟩: meet the requirements for *Tablets*.

Salicylic acid—

Solvent mixture, *Mobile phase*, *Internal standard solution*, and *Chromatographic system*—Prepare as directed in the *Assay*.

Procedure—Dissolve a suitable quantity of USP Salicylic Acid RS, accurately weighed, in *Solvent mixture* to obtain a solution having a known concentration of about 1.0 mg per ml. Transfer 1.0-ml, 5.0-ml, and 10.0-ml portions, respectively, of this solution to separate 100-ml volumetric flasks, add 10.0 ml of *Internal standard solution* to each flask, dilute with *Solvent mixture* to volume, and mix. Chromatograph these three Standard solutions as directed in the *Assay*. Plot the ratios of the peak responses for salicylic acid and benzoic acid for each of the Standard solutions versus concentrations, in mg per ml, of salicylic acid, and draw the straight line best fitting the three plotted points. From the graph so obtained, and from the ratio of the peak responses for salicylic acid and benzoic acid in the chromatogram of the *Assay preparation* as obtained in the *Assay*, determine the concentration, in mg per ml, of salicylic acid ($C_7H_6O_3$) in the *Assay preparation*, and calculate the percentage of salicylic acid in relation to the concentration of aspirin in the *Assay preparation*, as determined in the *Assay*. Not more than 3.0% is found.

Assay—[NOTE—Use clean, dry glassware. Inject the *Standard preparation* and the *Assay preparation* promptly after preparation.]

Solvent mixture—Prepare a mixture of chloroform, methanol, and glacial acetic acid (78:20:2).

Mobile phase—Transfer 225 mg of tetramethylammonium hydroxide pentahydrate to a 1000-ml flask, and add 750 ml of water, 125 ml of methanol, 125 ml of acetonitrile, and 1.0 ml of glacial acetic acid. Stir for 3 minutes, filter through a membrane filter (0.5-μm or finer porosity), and degas.

Internal standard solution—Dissolve benzoic acid in *Solvent mixture* to obtain a solution having a concentration of about 20 mg per ml.

Standard preparation—Transfer about 325 mg of USP Acetaminophen RS and about 325 mg of USP Aspirin RS, each accurately weighed, to a 100-ml volumetric flask, add 10.0 ml of *Internal standard solution*, dilute with *Solvent mixture* to volume, and mix.

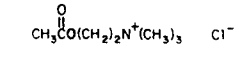
Assay preparation—Weigh and finely powder not less than 20 Acetaminophen and Aspirin Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 325 mg of acetaminophen, to a 100-ml volumetric flask, add 10.0 ml of *Internal standard solution* and about 50 ml of *Solvent mixture*, and sonicate for about 3 minutes. Dilute with *Solvent mixture* to volume, and mix. Filter a portion of this solution through a 2.5-μm or finer porosity filter, and use the filtrate as the *Assay preparation*.

Chromatographic system—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 ml per minute. Chromatograph four replicate injections of the *Standard preparation*, and record the peak responses as directed under *Procedure*: the relative standard deviation for either analyte is not more than 3.0%.

Procedure—Separately inject equal volumes (about 5 μl) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The retention times are about 2, 3, 5, and 8 minutes for acetaminophen, salicylic acid (if present), aspirin, and benzoic acid, respectively. Calculate the quantity, in mg, of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken by the formula $100C(R_U/R_S)$, in which C is the concentration, in mg per ml, of USP Acetaminophen RS in the *Standard preparation*, and R_U and R_S are the ratios of the peak responses of acetaminophen and benzoic acid obtained with the *Assay preparation* and the *Standard preparation*, respectively. Calculate the quantity, in mg, of aspirin ($C_9H_8O_4$) in the portion of Tablets taken by the same formula, except to read "USP Aspirin RS" where "USP Acetaminophen RS" is specified, and "aspirin" where "acetaminophen" is specified. ■4

Add the following:

■Acetylcholine Chloride



$C_7H_{16}ClNO_2$ 181.66

Ethanaminium, 2-(acetyloxy)-*N*,*N*,*N*-trimethyl-, chloride.

Choline chloride, acetate.

(2-Hydroxyethyl)trimethylammonium chloride, acetate [*60-31-1*].

» Acetylcholine Chloride contains not less than 98.0 percent and not more than 102.0 percent of $C_7H_{16}ClNO_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

Reference standard—*USP Acetylcholine Chloride Reference Standard*—Dry at 105° for 3 hours before using.